premature ventricular beats of ex vivo heart, under the acute adrenergic challenge, they significantly enhanced the frequency of premature ventricular beats.

**Conclusions** BPA promotes arrhythmogenesis in female rat heart by induced DADs, and effects of BPA and E2 are synergistic instead of additive.

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**e0181** RENALASE DEFICIENCY IN HEART FAILURE—A NOVEL MECHANISM UNDERLYING CIRCULATING NOREPINEPHRINE ACCUMULATION

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**Background** Sympathetic overactivity and catecholamine accumulation are important characteristic findings in heart failure, which contribute to its pathophysiology. However, the mechanism underlying circulating catecholamine accumulation remains largely unclear.

**Objective** To identify a novel mechanism underlying norepinephrine accumulation in a rat model of heart failure.

**Methods and results** Initially, we constructed a rat model of unilateral renal artery stenosis and found that the expression of renalase, a previously identified secreted amine oxidase, was markedly reduced in the ischemic compared to the non-ischemic kidney. Subsequently, we utilised an isolated perfused rat kidney model to demonstrate that the clearance rate of norepinephrine decreased with reduction of either perfusion flow or pressure. On the basis of these findings, we hypothesised that the reduced renal blood supply which occurs in heart failure would result in impaired synthesis of renalase by the kidney and consequently reduced degradation of circulating norepinephrine. To verify this, we used a rat model of infarction-induced heart failure caused by ligation of the left anterior descending coronary artery. In these rats, renal expression of renalase, when measured at 4 weeks, was reduced, and this was associated with an increase in circulating norepinephrine.

**Conclusions** We conclude that impaired synthesis of renalase by the kidney may represent a novel mechanism underlying circulating norepinephrine accumulation in heart failure.

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**e0182** ELECTROPHYSIOLOGICAL SUBSTRATE FOR CANINE ATRIUM

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**Objective** Hypertension is frequently complicated by atrial fibrillation (AF). However, the atrial substrate for AF is not known. This study investigated the electrophysiological properties of atrial repolarisation by monophasic action potential (MAP) in order to explore the mechanism of paroxysmal AF initiation and maintenance.

**Methods** MAP were recorded from left and right atrium in 14 canine action potential duration (APD) at 90% repolarisation (APD90). Repetitive atrial firing (RAE) the occurrence of two or more successive premature atrial activations with return cycle of 250 msec or less following atrial stimulation) and APD alternans (the difference in APD between two consecutive beats, were induced by overdrive pacing at LA and RA) were induced by use of programmed stimulation at LA and RA. In the study, episodes of PAF were recorded and analysed.

**Results** APD90 were significantly shorter in the left atrium compared to the right atrium ((157.4±43.5) vs (170.9±37.9), p<0.05). The mean S1S2 interval induced RAE was (150±52) ms. 15 RAE were induced in 14 dogs. RAE induced in LA were more than in RA (11 vs 4, p<0.05). Alternans of APD were induced at CL of (162±25) ms. 13 APD alternans were induced at LA (8) and RA (5) of 14 dogs. In total, 61 episodes of PAF were induced in 14 canines. 38 episodes of PAF were induced in the left atrium, more than in the right atrium (23, p<0.05).

**Conclusions** The incidence of RAE and alternans was significantly higher in LA than in RA. Heterogeneity between LA and RA repolarisation creates substrate for re-entrant arrhythmias and vulnerability to atrial fibrillation.

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**e0183** LIVIN PROTECTS AGAINST CARDIOMYOCYTE APOPTOSIS IN ANOXIA/REOXYGENATION INJURY VIA P38-MEDIATED SIGNAL PATHWAY

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**Introduction** Although anoxic preconditioning (APC) in the myocardium has been investigated for many years, its physiological mechanism is still not completely understood. Increasing evidence indicates that transiently increased resistance to ischemic damage following APC is dependent on de novo protein synthesis. However, the key effector pathway(s) associated with APC still remains unclear. Livin, a member of the inhibitor of apoptosis protein (IAP) family, since IAP-mediated activation of JNK1, as well as protection against TNF-β and ICE-induced apoptosis. The detailed mechanism underlying its antiapoptotic function in cardiomyocytes has not yet been fully characterised.

**Objective** To investigate whether Livin expression might be aberrantly induced in cardiomyocytes that were subjected to anoxia/ reoxygenation (A/R) injury and to investigate whether Livin might also contribute to cardio-protection after APC.

**Methods** We cloned a Livin expression vector, transfected it into rat cardiomyocytes, and examined Livin expression in rat cardiomyocytes that were subjected to A/R injury. Moreover, we studied the role of three major MAPK pathways, for example, p38 MAPK, JNK, and ERK1/2, in order to evaluate the molecular mechanism underlying Livin up-regulation and A/R induced cardiomyocyte injury.

**Results** APC induced an up-regulation of Livin and the transfection of Livin gene into the cardiomyocytes attenuated A/R injury. The inhibition of p38 MAPK by SB203580 abolished both the Livin up-regulation and the cardio-protection provided by APC.

**Conclusion** APC could act to protect the heart from A/R injury with cooperation from the Livin in addition, it up-regulates Livin expression through a p38 MAPK signalling pathway.

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**e0184** THE PROTECTION EFFECTS OF TRIMETAZIDINE ON RATS MYOCARDIAL INFRACTION

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**Objective** To observe the myocardial protection effects of trimetazidine on Sprague-Dawley (SD) rats with myocardial infarctions (MI).

**Methods** 90 SD rats were randomly assigned to normal control group (NL, n=30), Trimetazidine group (T, n=30) and sham-operated group (S, n=30). Trimetazidine 0.5mg/kg was infused into ventricle via tail vein at 7 days after ischemia. After 24 hours of reperfusion and 7 days of treatment, the heart was removed for further observation. The myocardial damage was evaluated by the area at risk (AAR), infarcted area (IA) and left ventricular ejection fraction (LVEF).

**Results** The administration of trimetazidine could significantly reduce the myocardial infarction (p<0.01). The area at risk was (60.0±5.8)% in the normal control group (N), (74.0±7.2)% in the sham-operated group (S), and (30.9±3.1)% in the trimetazidine group (T) (p<0.01). The infarcted area was (25.0±3.5)% in the normal control group (N), (32.0±4.8)% in the sham-operated group (S), and (15.0±2.2)% in the trimetazidine group (T) (p<0.01). The left ventricular ejection fraction was (60.0±5.0)% in the normal control group (N), (48.0±5.3)% in the sham-operated group (S), and (74.0±4.8)% in the trimetazidine group (T) (p<0.01).